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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/661,927	09/14/2000	William J. Dower	019282-000110US	1158

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EXAMINER
EPPERSON, JON D

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 07/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/661,927	DOWER ET AL.	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-77* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,14,25-29,49,56 and 66* is/are rejected.

7)☒ Claim(s) *15,16,30-35,37,40,46-48,50,52-54,58 and 68* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 4-13,17-24,36,38,39,41-45,51,55,57,59-65,67 and 69-77.

DETAILED ACTION

Status of the Application

1. The Response filed April 10, 2006 is acknowledged.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

Status of the Claims

3. Claims 1 and 3-77 were pending. No claims were amended, added or canceled. Therefore, claims 1 and 3-77 are currently pending. Claims 4-13, 17-24, 36, 38, 39, 41-45, 51, 55, 57, 59-65, 67 and 69-77 are drawn to non-elected species and/or inventions and thus these claims remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), there being no allowable generic claim. Therefore, claims 1, 3, 14, 15, 16, 25-35, 37, 40, 46-50, 52-54, 56, 58, 66 and 68 are examined on the merits.

Withdrawn Objections/Rejections

4. All rejections are maintained and the arguments are addressed below.

Outstanding Objections and/or Rejections

Claims Rejections - 35 U.S.C. 102

5. Claims 1 and 3, 14, 25-29, 49, 56 and 66 are rejected under 35 U.S.C. 102(b) as being anticipated by Swanson et al. (Swanson, S. J.; Bethke, P.; Jones, R. L. "Barley Aleurone Cells

Contain Two Types of Vacuoles: Characterization of Lytic Organelles by Use of Fluorescent Probes" *The Plant Cell* **May 1998**, *10*, 685-698) (of record) as evidenced by Ozkan et al. (Ozkan P.; Mutharasan, R. "A rapid method for measuring intracellular pH using BCECF-AM" *Biochim. Biophys. Acta.* **2002**, *1572*, 143-148) (of record).

For ***claims 1, 56 and 66***, Swanson et al. (see entire document) disclose the use of a library of fluorescent conjugates in screening and/or characterizing two forms of vacuoles, protein storage vacuoles and secondary vacuoles, in protoplasts of barley aleurone (e.g., see Swanson et al., abstract; see also Table 1), which anticipates the claimed invention. For example, Swanson et al. disclose providing a library comprising different complexes, each complex comprising a compound and a reporter, the compound varying between different complexes (e.g., see Table 1). For example, Swanson et al. disclose the use of BCECF-AM, ZFR-GMAC, and ZFR-CMAC-GS (e.g., see Table 1, see also figure 4; see also pages 687-688) wherein the different compound represents the "AM" or "ZFR" portions and the reporter represents the cleaved "BCECF" or the "CMAC-GS" (e.g., see figure 4; see also Table 1; see also figure 3; see also discussion; see also Ozkan et al., poage 143, column 2, paragraph 1, disclosing cleavage mechanism for BCECF-AM, "… intracellular esterases cleave the ester bond releacing BCECF, which fluoresces according to the intrcellular pH"). Please note that many other compounds can fall within the scope of the library like the glutathione/sulfhydryl conjugates (e.g., see Table 1). In addition, providing a population of living barley aleurone cells, one or more of which expresses one or more carrier-type transport proteins including organic anion transporter and glutathione conjugate transporter (e.g., see

abstract wherein cells are disclosed; see also page 686, column 1, last paragraph; see also page 695, column 1, paragraph 2, "we conclude that at least two kinds of ATP-dependent transporters are present in protein storage vacuoles. One of these is an organic anion transporter that can be inhibited by probenecid and transports BCECF. The other is a glutathione conjugate transporter that is not inhibited by probenecid and transports MCB-GS. Both transporters may belong to the superfamily of ABC transporters"). In addition, the cells were contacted with the library members (e.g., see figures showing uptake of various conjugates). Furthermore, Swanson et al. disclose detecting a signal from the reporter of a complex while internalized within a cell, wherein the reporter preferentially generates the signal once the reporter is internalized within a cell rather than from complexes binding to the surface of the cell, the signal thus providing an indication that a complex whose reporter generated the signal comprises a compound that is a substrate for a carrier-type transport protein (e.g., see figure 4 showing preferential generation of signal for proteolytically cleaved ZFR-CMAC-GS; see also discussion with regard to ZFR-GMAC-GS and conclusion identifying this compound as a substrate for a glutathione conjugate transporter that is a member of the ABC superfamily e.g., see page 695, column 1, paragraph 1). In addition, Swanson et al. disclose that the fluorophores is linked to a quencher by a linker susceptible to cleavage within the cell, whereby the quencher quenches fluorescence from the fluorophores outside the cell and is cleaved from the fluorophores within the cell after the complex is internalized within the cell, whereby the reporter preferentially generates the signal once internalized within the cell (e.g., see figure 4 showing preferential cleavage of ZFR-GMAC-GS to GMAC-GS

wherein a signal is preferentially generated upon internalization; see also Ozkan et al., page 143, column 2, paragraph showing that BCECF-AM is cleaved to BCECF for signal generation upon internalization of BCECF-AM into the cell; see also figures in Swanson et al. showing results of conjugate uptake).

For ***claims 3 and 14***, Swanson et al. disclose the enzymatic cleavage of ZFR-CMAC-GS to GMAC-GS substrates (e.g., see figure 4; see also page 688, column 1, last paragraph; see also Ozkan et al., page 143, column 2, paragraph 1).

For ***claims 25-28***, Swanson et al. disclose both protein storage and lysosome-like secondary vacuoles, which can be considered a population of cells or, alternatively, the population of cells is differentiated by the addition of (e.g., see figures 1 and 4 showing hormone treatments) or, alternatively, the cells are different based on the addition of various inhibitors and compared to as compared to a control cell wherein the identity of various cells is determined by microscopy (e.g., see figure 9).

For ***claim 29***, Swanson et al. disclose cells with different cellular morphologies (e.g., see figure 1 showing differentiation of morphology of protein storage vacuoles versus secondary vacuoles; see also page 686, column 2, last paragraph).

For ***claim 49***, Swanson et al. disclose, for example, an organic anion transporter (e.g., see page 695, column 1, paragraph 2).

Response

6. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed

persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue that Swanson et al. do not teach the limitation of providing a library comprising different complexes because Swanson et al. set forth "only one complex" i.e., ZFR-CMAC-GS. Applicants further state that the other complexes like BCECF-AM do not constitute "complexes" as defined in the claims and specification because they do not possess the requisite "substrate-reporter-quencher" structure (e.g., see 4/10/06 Response, pages 16 and 17, especially page 17).

[2] Applicants argue, "Swanson et al. does not disclose the step of "contacting the population of cells with a plurality of complexes from the library" because the only complex that Swanson discusses that arguably fits the claimed definition is produced intracellularly. The cells are not contacted with complex because the complex is not formed until the reporter/quencher agent enters the cell" (e.g., see 4/10/06 Response, bottom of page 17 and top of page 18).

This is not found persuasive for the following reasons:

[1] In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (e.g., substrate-reporter-quencher) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Here, Applicants claims merely require that the library members contain a "compound and a reporter" (e.g., see claim 1, step (a)). Consequently, the only structure required by the claim is compound-reporter, not

substrate-reporter-quencher as purported by Applicants. In fact, the claim is drawn to a method of screening for a substrate and, as a result, a person of ordinary skill in the art would expect that many of the library members would not be "substrates" at all (i.e., the whole purpose of the method is trying to differentiate those compounds that do act as substrates from those that do not). Furthermore, nothing in the claims rules out the possibility that the compound portion of the compound-reporter library represents the quencher, or both the quencher and the substrate at the same time (i.e., plays a dual role), or that the "substrate" is the "compound-reporter" in its entirety. That is, the claim doesn't read "(a) providing a library comprising different complexes, each complex comprising a substrate and a reporter", nor does the claim read "(a) providing a library comprising different complexes, each complex comprising a compound that cannot function as a quencher and a reporter." Therefore, Applicants' arguments are not commensurate in scope with the claims.

[2] Again, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (e.g., "extracellular" contact) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Here, the claims only require that the population of cells be "contacted" with the plurality of complexes from the library, not "contacted extracellularly" as purported by Applicants. Therefore, it does Applicants' arguments are moot. Furthermore, the ZFR-CMAC and ZFR-GMAC-GS as shown in figure 4 are contacted "extracellularly" with respect to the vacuole that contain the transporter. Finally, as discussed above, the library members only require a compound-reporter structure

(e.g., see **[1]** above) and, as a result, both ZFR-CMAC and ZFR-GMAC-GS, for example, represent two members of the library where the different compounds are CMAC and CMAC-GS.

Accordingly, the 35 U.S.C. 102 rejection cited above is hereby maintained.

Allowable Subject Matter

7. Claim 15, 16, 30-35, 37, 40, 46-48, 50, 52-54, 58 and 68 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
July 8, 2006

JON EPPERSON, PH.D.
PATENT EXAMINER